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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/716,095

11/18/2003

Alexandra Kaczmarek

21489

5755

151 7590 10/07/2008  
HOFFMANN-LA ROCHE INC.  
PATENT LAW DEPARTMENT  
340 KINGSLAND STREET  
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EXAMINER

PARKIN, JEFFREY S

ART UNIT

PAPER NUMBER

1648

MAIL DATE

DELIVERY MODE

10/07/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/716,095	<b>Applicant(s)</b> KACZMAREK ET AL.	
	<b>Examiner</b> Jeffrey S. Parkin, Ph.D.	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 July 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**Detailed Office Action**

***Status of the Claims***

Acknowledgement is hereby made of receipt and entry of the communication filed 01 July, 2008. Claims 1-5 are pending in the instant application.

***35 U.S.C. § 103(a)***

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Amended claims 1-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Oldenburg et al. (1994) in view of Lambert et al. (2000), Mukhopadhyay (1997), and Vendenbark (1997). As previously set forth, Oldenburg and colleagues disclose a recombinant parathyroid hormone analog, rPTH(1-34\*), was obtained from Escherichia coli using a gene polymerization strategy. The PTH gene polymer contains up to 8 copies of the gene, each separated by a cleavable linker. **The polymer was expressed at very high levels and formed inclusion bodies which could be easily isolated by low-speed centrifugation. A polyhistidine leader peptide allows rapid purification via**

nickel chelation chromatography of the PTH polymer solubilized from the inclusion bodies. Yields of greater than 500 mg/liter have been obtained. After isolating the polymer, monomeric rPTH(1-34\*) is released from the polymer by chemical cleavage with cyanogen bromide. Following cyanogen bromide cleavage and high-performance liquid chromatography purification, highly purified, biologically active rPTH(1-34\*) is obtained at a yield of approximately 300 mg/liter. This teaching provides a general strategy for the high-level production of a variety of peptides and small proteins using inclusion bodies. This teaching does not provide antifusogenic polypeptides.

Lambert and colleagues provide a number of antifusogenic peptides comprising DP178 (aa 638-673). These peptides are potent inhibitors of HIV-1 replication.

Mukhopadhyay (1997) provides a detailed review concerning the purification of proteins from inclusion bodies. Various formats are disclosed including the utilization of a denaturing agent at the recited range.

Finally, Vandenbark (1997) teaches the inclusion of C-terminal glycine residues in polypeptides is useful because it facilitates their conjugation to other carrier molecules or it facilitates their synthesis during solid-phase syntheses.

Therefore, it would have been *prima facie* obvious at the time of the invention to utilize the polypeptide inhibitors of Lambert et al. (2000), in the protocols of Oldenburg et al. (1994), since this would facilitate the high-level production of

purified peptide. One of ordinary skill in the art would also be motivated to employ the purification protocols provided by Mukhopadhyay (1997), since this would also facilitate the high-level production of peptide. One of ordinary skill in the art would have been further motivated to incorporate a C-terminal Gly, as taught by Vandenbark (1997), to facilitate the synthesis of the fusion peptides or the conjugation to a carrier molecule.

*Response to Arguments*

Applicants argue, *inter alia*, that the prior art fails to teach or suggest the inclusion of a C-terminal Gly or a washing step at a pH of less than or equal to 6.5. First, Vandenbark (1997) provides the motivation for modifying polypeptides to include a C-terminal Gly since this will facilitate their synthesis or conjugation to a carrier molecule. Second, Mukhopadhyay (1997) provides a detailed review concerning inclusion body purification protocols and discusses utilizing a range of pH values (see pp. 85-86). Although a specific wash employing a pH of 6.5 is not disclosed, nevertheless, this teaching discloses that different pHs and other conditions may be employed depending upon the individual characteristics of the protein. Thus, all that is required to arrive at the claimed invention is routine experimentation.

Applicants are reminded that generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the

optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 U.S.P.Q. 233, 235 (C.C.P.A. 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 U.S.P.Q.2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 U.S.P.Q. 809 (C.C.P.A. 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 U.S.P.Q.2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 U.S.P.Q.2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 U.S.P.Q.2d 1362 (Fed. Cir. 1997).

### ***Action Is Final***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

### ***Correspondence***

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may

**Application No.: 10/716,095**

**Docket No.: 21489**

**Applicants: Kaczmarek, A., et al.**

**Filing Date: 11/18/2003**

be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin, Ph.D./  
Primary Examiner, Art Unit 1648

30 September, 2008